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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/751,088	01/02/2004	Alexander Knuth	NY-LUD-5466.8-DIV	2148
24972	7590	01/13/2006	EXAMINER	
FULBRIGHT & JAWORSKI, LLP 666 FIFTH AVE NEW YORK, NY 10103-3198			VANDERVEGT, FRANCOIS P	
			ART UNIT	PAPER NUMBER
			1644	

DATE MAILED: 01/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.		Applicant(s)	
	10/751,088		KNUTH ET AL.	
	Examiner		Art Unit	
	F. Pierre VanderVegt		1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 74-94 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 89-92 is/are allowed.
- 6) ☒ Claim(s) 74-78,81-88,93 and 94 is/are rejected.
- 7) ☒ Claim(s) 79-80 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

This application is a divisional of U.S. Application Serial Number 09/165,546, which is a continuation-in-part of U.S. Application Serial Number 09/062,422, which is a continuation-in-part of U.S. Application Serial Number 08/937,263, which is a continuation-in-part of U.S. Application Serial Number 08/725,182.

Claims 1-73 have previously been canceled.

New claims 74-94 have previously been added and are currently pending.

Applicants amendment filed October 11, 2005 has been fully considered. In view of Applicant's amendment no outstanding grounds of rejection have been maintained.

The following represent new grounds of rejection not necessitated by Applicant's amendment. Accordingly, this Office Action is made NON-FINAL.

Claim Objections

1. Claim 75 is objected to under 37 CFR 1.75 as being a duplicate of claim 74. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 74-78 and 81-87 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to an isolated nucleic acid molecule that encodes a polypeptide consisting of an unspecified immunoreactive portion of a protein encoded by SEQ ID NO: 1. it is noted

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that SEQ ID NO: 1 is a nucleic acid sequence that encodes the NY-ESO-1 protein of SEQ ID NO: 15. The claim includes nucleic acid sequences encoding any two or more consecutive amino acid residues that an immune response could be raised against. Given that the nucleic acid is being defined in terms of a sequence that is complementary to a sequence that binds to SEQ ID NO: 1 under particular hybridization conditions, the claimed sequence may also encode for amino acid residues that are not defined by the amino acid sequence encoded by SEQ ID NO: 1, i.e., conservative or non-conservative substitutions and/or additions, this broadens the claims to include sequences that encode immunogenic portions of proteins other than the NY-ESO-1 protein disclosed in the specification as originally filed. There is no support in the specification for nucleic acid sequences that encode immunogenic polypeptides of proteins other than the disclosed NY-ESO-1 sequence of SEQ ID NO: 15. However, there is no disclosure of immunogenic polypeptides from protein sequences other than those obtained from SEQ ID NO: 15 and the only immunogenic sequences thereof that are described are those enumerated in the specification as SEQ ID NO: 4-13. Therefore, the only nucleic acid molecules encoding immunoreactive portions of a protein that been adequately described by the instant specification are those that encode fragments of SEQ ID NO: 15 comprising or consisting of a sequence selected from the group consisting of SEQ ID NO: 4-13.

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111) clearly states that “Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See *Vas-Cath* at page 1117). The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see *Vas-Cath* at page 1115).

The detailed structure of the encompassed nucleic acid molecules encoding an immunoreactive polypeptides encoded by the complementary sequence to one that hybridizes to SEQ ID NO: 1 under claimed hybridization conditions has not been described for nucleic acid molecules that encodes polypeptides other than fragments of SEQ ID NO: 15 comprising a sequence selected from the group consisting of SEQ ID NOs: 4-13. Therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, ((CAFC, 1993) 25 USPQ 2d 1601) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, ((CAFC, 1991) 18 USPQ2d 1016).

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See also, the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

3. Claim 88 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claim is broadly drawn to the prevention of a cancerous condition by administering a vector encoding an immunogen to a subject, wherein the immunogen is an 18-25 amino acid residue fragment of SEQ ID NO: 15. The nature of the claimed method, therefore, is one of immunotherapeutic intervention. While the specification is vague about the purpose of administering the vector (page 33, line 26 through page 34, line 4 for example), the apparent aim of administering the vector to a subject prophylactically would be to serve to raise an immune response to the encoded peptide such that immune cells of the subject can recognize and eliminate cancer cells.

As a first matter, there is no restriction regarding the type of cancerous condition being treated. The claim treats all cancerous conditions, irrespective of whether the cancerous condition would express antigens related to peptides of SEQ ID NO: 15. Even assuming that the vectors of the instant claim would be able to express a recognizable immunoepitope *in vivo*, the vectors of the instant claim would not be recognized by the artisan as being able to stimulate an immune response to peptides other than those contained within SEQ ID NO: 15. there is no disclosure in the instant specification regarding cross-reactivity of the immune response to SEQ ID NO: 15 with the response to other cancer related antigens. Furthermore, it is well known in the art that not all tumors express the same antigens. Indeed, even the instant specification recognizes that SEQ ID NO: 15 is not even expressed by all melanoma tumors (page 15, lines 1-14 for example).

Furthermore, the instant specification does not provide any indication regarding the ability of immunotherapeutic methods using the vectors of the claim to prevent any type of tumor. Despite many years of research on the subject, immunotherapeutic methods for the prevention of cancer remain unpredictable in the art and, while working examples are not required in an application for a patent, in an unpredictable art there is a need for sufficient guidance from the specification in order for the artisan to predict the efficacy of the claimed method.

Bodey (Anticancer Research [2000] 20:2665-2676; U on form PTO-892, newly cited) discloses, “[I]t has been over a century since William Coley’s first report of cancer regressions induced by immune system activation in response to bacterial toxins. While many cancer vaccine trials have yielded tantalizing results, active immunotherapy has not yet become an established modality of anticancer therapy” (page 2665, 2nd column in particular). Bodey also discloses, “[t]he failure of cancer vaccines to fulfil their promise is due to the very relationship between host and tumor: through a natural selection process the host leads to the selective enrichment of clones of highly aggressive neoplastically transformed cells, which are apparently so dedifferentiated that they no longer express cancer cell specific molecules. Specific activation of the immune system in such cases only leads to lysis of the remaining cells expressing the particular TAAs in the context of the particular human leukocyte antigen (HLA) subclass and the necessary costimulatory molecules. The most dangerous clones of tumor cells however lack these features and thus the cancer vaccine is of little use” (Abstract in particular). accordingly, the instant method of preventing cancer by administering vectors which express immunoepitopes of NY-ESO-1 would be predicted by those in the art to cause the selection of more aggressive tumor cells that escape detection by the immune system via the suppression of TAA expression.

Marchand (Int. J. Cancer [1999] 20:219-230; V on form PTO-892, newly cited) discloses in her conclusion, “[c]onsiderable further progress is needed...before immunization with tumor-specific antigens recognized by T cells becomes an effective and generally applicable cancer therapy” (page 229, 2nd column in particular). Marchand (Exp. Opin. Biol. Ther. [2001] 1(3):497-510; W on form PTO-892, newly cited) subsequently discloses, “[I]t is fair to say that in patients vaccinated with defined antigen, the immune responses induced have been so far very poor, if present. In some studies, immune responses were reported for some patients but without any correlation with the clinical responses. In addition, some patients with complete and long-term regressions of several melanoma metastases failed to mount a detectable response against the antigen present in the vaccine” (page 505, 2nd column, last paragraph in particular). Therefore, even when the antigen used in an active immunotherapeutic method, such as the method instantly claimed, is known to be related to the type of cancer for which treatment or prevention is

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sought, there is often little to no correlation between the immune response to the antigen and the clinical status of the patient.

In view of the limited guidance provided by the specification, the level of unpredictability in the art, the nature of the claimed invention and the undue experimentation required of one of ordinary skill in the art, it would require an undue amount of trial and error to practice the full scope of the invention and this is not sanctioned by the statute.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 93-94 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 93 recites the limitation "the complex of claim 90" in line 2. There is no antecedent basis for this limitation in the claim. Claim 90 does not recite any type of complex.

Conclusion

5. Claims 79 and 80 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. Claims 89-92 are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
January 9, 2006

David A. Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
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